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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/678,571	10/03/2003	Abubakr Aslamkhan	2187US	1231
22881	7590	08/23/2005	EXAMINER	
ERIC J. KRON ICORIA, INC. 108 T.W. ALEXANDER DRIVE, BUILDING 1A POST OFFICE BOX 14528 RESEARCH TRIANGLE PARK, NC 27709			WALICKA, MALGORZATA A	
			ART UNIT	PAPER NUMBER
			1652	
DATE MAILED: 08/23/2005				

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/678,571

Applicant(s)

ASLAMKHAN ET AL.

Examiner

Malgorzata A. Walicka

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-28 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-28 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. ____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. ____. |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date ____. | 6) <input type="checkbox"/> Other: ____. |

Claims 1-28 are pending and under examination.

Detailed Action

1. Objections

The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors in the specification of which Applicant may become aware.

2. Rejections

2.1. 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2.2.1. Written description

Claims 1-28 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are directed to genera of method for identifying inhibitors of obtusifoliosyl 14 α -demethylase (OBT-DM) wherein the methods comprise measuring the amplitude of the difference of absorbance around 432 nm and 413 nm in the presence of the test compound, and wherein an increase in the amplitude in the presence of the test compound indicates that the compound is an OBT-DM inhibitor. The claims are lacking sufficient written description for the following reasons. The claims are generic for any inhibitor, but not any inhibitor is suitable for the claimed methods of measurement. As applicants point on page 2 line 3, and 10, only inhibitors based on triazole or imidazole moiety, i.e., exhibiting "type II spectrum" can be tested by the claimed method. The disclosure does not provide support for the full scope of the claimed invention i.e. for identifying any inhibitor of OBT-DM. If a test-compound interacts with OBT-DM as its substrate does, and for that reason is an inhibitor, it exhibits type I substrate-binding spectrum (see Bak et al. Plant J. 1997, 11(2), 191). Because said compound exhibits spectrum type I when binding the enzyme it cannot be identified by the claimed method as an inhibitor, although it is an inhibitor.

Because the claimed invention is not fully supported by the disclosure, one skilled in the art is not convinced that applicants were in possession of the claimed invention at the time the application was filed.

2.2.3. Scope of enablement

Claim 1-28 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the method for identifying inhibitors exhibiting

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'type II spectrum", does not reasonably provide enablement for identifying any inhibitor. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Otherwise, undue experimentation is necessary to make the claimed invention.

Factors to be considered in determining whether undue experimentation is required are summarized *In re Wands* [858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)]. The Wands factors are: (a) the quantity of experimentation necessary, (b) the amount of direction or guidance presented, (c) the presence or absence of working example, (d) the nature of the invention, (e) the state of the prior art, (f) the relative skill of those in the art, (g) the predictability or unpredictability of the art, and (h) the breadth of the claim.

The nature and breath of the claimed invention encompasses genera of methods for identifying any chemical compound as an inhibitor of OBT-DM. The method, however, as taught by the Applicants; see the above rejection for lack of written description, applies only to the test compound having a particular chemical structure. Only inhibitors based on triazole or imidazole moiety, the interaction of which with the enzyme results in type II spectrum, can be used in the method.

Examiner concludes that without a further detailed guidance on the part of Applicants regarding the structure of the chemical tested in the method, experimentation left to those skilled in the art has a low probability of success and is undue.

3.3. 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 1 and 3 are rejected under 35 U.S.C. 102(b) as being anticipated by Lamb et al. (Plant Sterol 14alpha-Demethylase Affinity for Azole Fungicides, Biochem. Biophys. Res. Commun. 2001, 284, 845-849).

Claim 1 and 3 are directed to a method for identifying inhibitors of obtusifoliol 14alpha-demethylase (OBT-DM) wherein the methods comprises measuring the amplitude of the difference of absorbance around 432 nm and 413 nm in the presence of the test compound, wherein an increase in the amplitude in the presence of the test compound indicates that the compound is an OBT-DM inhibitor, wherein the enzyme is any OBT-DM or plant OBT-DM.

Lamb et al. examined whether fungicides triadimenol and tebuconazole inhibit PBT-DM from the plant *S. bicolor*. Lamb et al. used for this purpose spectral amplitudes (Fig. 2, page 847, left column), which were differences of absorption at the

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spectral peak maximum at 428-432 nm and spectral minimum at 413 nm. Their data from Fig. 3, page 847, right column, indicate that tebuconazole is a better inhibitor of the *S. bicolor* OBT-DM than triadimenol, because the amplitude of difference is greater for tebuconazole. The data obtained by calculating amplitudes were confirmed by direct enzymatic measurement of inhibitory concentration (IC_{50}) for both fungicides. IC_{50} was smaller for tebuconazole (Table 1, page 848, left column).

In conclusion, Lamb et al. teach the method claimed in claim 1 and 3 of the instant application.

3.4. 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 2, 4-8, 9-10, 11-19 and 20-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lamb et al. (Plant Sterol 14 α -Demethylase Affinity for Azole Fungicides, Biochem. Biophys. Res. Commun. 2001, 284, 845-849), in view of common knowledge in the field of biochemistry as exemplified by Garrigues A. et al. (A High-Throughput Screening Microplate Test for the Interaction of Drugs with P-glycoprotein, Analytical Biochemistry, 2002, 305, 106-114).

The claims are directed to methods for identifying inhibitors of obtusifoliosol 14 α -demethylase (OBT-DM) of different origin, using a multiwell format, wherein the methods comprise measuring the amplitude of the difference of absorbance around 432 nm and 413 nm in the presence of the test compound, wherein an increase in the amplitude in the presence of the test compound indicates that the compound is an OBT-DM inhibitor.

Lamb et al. examined whether fungicides triadimenol and tebuconazole inhibit PBT-DM from the plant *S. bicolor*. Lamb et al. used for this purpose spectral amplitudes (Fig. 2, page 847, left column), which were differences of absorption at the spectral peak maximum at 428-432 nm and spectral minimum at 413 nm. Their data from Fig. 3, page 847, indicate that the better inhibitor the greater the amplitude. Lamb et al. however do not teach their method in a multi-well format and for any PBT-DM.

The skill artisan realizes that multi-well, high through-put, format has been used in biomedical studies for more than 20 years now, because performing biochemical reactions in microplates and subsequently using microplate spectrophotometrical readers dramatically increases laboratory productivity when a large number of samples need to be analyzed. For example, Garrigues et al. teach a spectrophotometric method for identification of drug interaction with the P-glycoprotein in a high-throughput system format; see the abstract.

It would have been obvious to one having ordinary skills in the art at the time of invention, to use the method of Lamb et al. and adopt it to a multiwell high-throughput format as Garrigues et al. did. It would be also obvious for one of ordinary skill in the art

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to us the method to any PBT-DM. The motivation would be obvious for one having ordinary skills in the art and is provided by Garrigues et al. who state on page 106, left column, the first line under the abstract, "Due to the development of combinatorial chemistry, there is currently an emphasis on the use of high-throughput screening using *in vitro* models to characterize a potential new candidate drugs." The expectation of success is very high, because Garrigues tested using the multi-well format 41 chemicals, of which 9 occurred to be inhibitors of P-glycoprotein. Thus, the claimed invention was within the ordinary skill in the art to make and use at the time it was made and was as a whole, *prima facie* obvious.

4. Conclusion

All claims are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Malgorzata A. Walicka whose telephone number is (571) 272-0944. The examiner can normally be reached on Monday-Friday from 10:00 a.m. to 4:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, can be reached on (571) 272-0928. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.


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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Malgorzata A. Walicka, Ph.D.

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Patent Examiner



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